and HCDR3 residue arg^{101} interact co-operatively to enhance the affinity of the mAb (Schreiber & Fersht, (1995)). In addition, the co-operative interaction that was observed between tyr^{49} and arg^{101} was also observed for variants that expressed lysine at HCDR3 position 101 (Table II).

Generally, interacting residues are spatially separated by no more than 7 Å (Schreiber & Fersht, 1995)). Figure 3 shows molecular modeling of anti-CD40 variant CW43. A top view of the anti-CD40 variant CW43 variable region structure was created by homology modeling to examine the spatial relationship of L chain framework residue Y49 and H chain CDR3 residue R101. The L chain is on the left and the H chain right with the H chain CDR3 loop depicted in red. The L chain framework residue 49 is in close proximity to the H chain CDR3 loop and is 7Å of the predicted interacting H chain CDR3 R101 residue. Although the interacting amino acids are located on distinct chains of the mAb, the residues are predicted to be within a range (7 Å) to permit co-operative interaction.

Throughout this application various publications have been referenced within parentheses. The disclosures of these publications in their entireties are hereby incorporated by reference in this application in order to more fully describe the state of the art to which this invention pertains.

Although the invention has been described with reference to the disclosed embodiments, those skilled in the art will readily appreciate that the specific experiments detailed are only illustrative of the invention. It should be understood that various

modifications can be made without departing from the spirit of the invention. Accordingly, the invention is limited only by the following claims.